

SEQUENCE LISTING

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<120> MODULATION OF EPIDERMAL GROWTH FACTOR HETERODIMER ACTIVITY

<130> 421/99 PCT/US

<150> US 60/545,185
<151> 2004-02-17

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<170> PatentIn version 3.3

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Lys	Arg	Pro	Ala	Gly	Ser	Val	Gln	Asn	Pro	Val	Tyr	His	Asn	Gln	1100	1105	1110	
Pro	Leu	Asn	Pro	Ala	Pro	Ser	Arg	Asp	Pro	His	Tyr	Gln	Asp	Pro	1115	1120	1125	
His	Ser	Thr	Ala	Val	Gly	Asn	Pro	Glu	Tyr	Leu	Asn	Thr	Val	Gln	1130	1135	1140	
Pro	Thr	Cys	Val	Asn	Ser	Thr	Phe	Asp	Ser	Pro	Ala	His	Trp	Ala	1145	1150	1155	
Gln	Lys	Gly	Ser	His	Gln	Ile	Ser	Leu	Asp	Asn	Pro	Asp	Tyr	Gln	1160	1165	1170	
Gln	Asp	Phe	Phe	Pro	Lys	Glu	Ala	Lys	Pro	Asn	Gly	Ile	Phe	Lys	1175	1180	1185	
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Lys Tyr Ala Asp Ala Asn Asn Val Cys His Leu Cys His Ala Asn Cys
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Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Lys Tyr
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Gln Cys Cys His Asp Glu Cys Ala Gly Gly Cys Ser Gly Pro Gln Asp
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Thr Asp Cys Phe Ala Cys Arg His Phe Asn Asp Ser Gly Ala Cys Val
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Glu Pro Asn Pro His Thr Lys Tyr Gln Tyr Gly Gly Val Cys Val Ala
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 cta aac ggg ctg agt gtg acc ggc gat gct gac aac cag tac cag aca 144
 Leu Asn Gly Leu Ser Val Thr Gly Asp Ala Asp Asn Gln Tyr Gln Thr
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 ctg tac aaa ctc tat gag aag tgt gag gtg gtc atg ggt aac ctg gag 192
 Leu Tyr Lys Leu Tyr Glu Lys Cys Glu Val Val Met Gly Asn Leu Glu
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 Ile Val Leu Thr Gly His Asn Ala Asp Leu Ser Phe Leu Gln Trp Ile
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 Arg Glu Val Thr Gly Tyr Val Leu Val Ala Met Asn Glu Phe Ser Val
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ctg ccc tta cct aac ctc cga gtg gtc cgg gga acc cag gtc tac gat	336
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Gly Lys Phe Ala Ile Phe Val Met Leu Asn Tyr Asn Thr Asn Ser Ser	
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His Ala Leu Arg Gln Leu Arg Phe Thr Gln Leu Thr Glu Ile Leu Leu	
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Glu Pro Asn Pro His Ile Lys Tyr Gln Tyr Gly Gly Val Cys Val Ala	
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Ser Trp Pro Pro His Met His Asn Phe Ser Val Phe Ser Asn Leu Thr
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Arg Leu Asp Ile Lys Tyr Asn Arg Pro Leu Gly Glu Cys Val Ala Glu
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Gly Lys Val Cys Asp Pro Leu Cys Ser Ser Gly Gly Cys Trp Gly Pro
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His Glu Ala His Cys Phe Ser Cys His Pro Glu Cys Gln Pro Met Glu
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Val Cys Ile Lys Val Ile Glu Asp Lys Ser Gly Arg Gln Ser Phe Gln
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 Ser Asp Leu Glu Gln Gln Tyr Arg Ala Leu Arg Lys Tyr Tyr Glu Asn
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Gln Thr Phe Val Tyr Asn Pro Thr Thr Phe Gln Leu Glu His Asn Phe	
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Leu Arg Lys Tyr Tyr Glu Asn Cys Glu Val Val Met Gly Asn Leu Glu
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Arg Glu Val Thr Gly Tyr Val Leu Val Ala Leu Asn Gln Phe Arg Tyr
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Leu Pro Leu Glu Asn Leu Arg Ile Ile Arg Gly Thr Lys Leu Tyr Glu
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Asp Arg Tyr Ala Leu Ala Ile Phe Leu Asn Tyr Arg Lys Asp Gly Asn
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Phe Gly Leu Gln Glu Leu Gly Leu Lys Asn Leu Thr Glu Ile Leu Asn
130 135 140

Gly Gly Val Tyr Val Asp Gln Asn Lys Phe Leu Cys Tyr Ala Asp Thr
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Ile His Trp Gln Asp Ile Val Arg Asn Pro Trp Pro Ser Asn Leu Thr
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Leu Val Ser Thr Asn Gly Ser Ser Gly Cys Gly Arg Cys His Lys Ser
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Cys Thr Gly Arg Cys Trp Gly Pro Thr Glu Asn His Cys Gln Thr Leu
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Tyr Val Ser Asp Cys Cys His Arg Glu Cys Ala Gly Gly Cys Ser Gly
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 Pro Lys Asp Thr Asp Cys Phe Ala Cys Met Asn Phe Asn Asp Ser Gly
 245 250 255
 Ala Cys Val Thr Gln Cys Pro Gln Thr Phe Val Tyr Asn Pro Thr Thr
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 Cys Val Lys Lys Cys Pro His Asn Phe Val Val Asp Ser Ser Ser Cys
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 Val Arg Ala Cys Pro Ser Ser Lys Met Glu Val Glu Glu Asn Gly Ile
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 Lys Met Cys Lys Pro Cys Thr Asp Ile Cys Pro Lys Ala Cys Asp Gly
 325 330 335
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 340 345 350
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 Asp Pro Glu Lys Leu Asn Val Phe Arg Thr Val Arg Glu Ile Thr Gly
 385 390 395 400
 Phe Leu Asn Ile Gln Ser Trp Pro Pro Asn Met Thr Asp Phe Ser Val
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 Phe Ser Asn Leu Val Thr Ile Gly Gly Arg Val Leu Tyr Ser Gly Leu
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 Ser Leu Lys Glu Ile Ser Ala Gly Asn Ile Tyr Ile Thr Asp Asn Ser
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Asn Leu Cys Tyr Tyr His Thr Ile Asn Trp Thr Thr Leu Phe Ser Thr
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Ile Asn Gln Arg Ile Val Ile Arg Asp Asn Arg Lys Ala Glu Asn Cys
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Thr Ala Glu Gly Met Val Cys Asn His Leu Cys Ser Ser Asp Gly Cys
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Trp Gly Pro Gly Pro Asp Gln Cys Leu Ser Cys Arg Arg Phe Ser Arg
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Gly Arg Ile Cys Ile Glu Ser Cys Asn Leu Tyr Asp Gly Glu Phe Arg
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Glu Phe Glu Asn Gly Ser Ile Cys Val Glu Cys Asp Pro Gln Cys Glu
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Lys Met Glu Asp Gly Leu Leu Thr Cys His Gly Pro Gly Pro Asp Asn
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Cys Thr Lys Cys Ser His Phe Lys Asp Gly Pro Asn Cys Val Glu Lys
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Cys Pro Asp Gly Leu Gln Gly Ala Asn Ser Phe Ile Phe Lys Tyr Ala
 595 600 605

Asp Pro Asp Arg Glu Cys His Pro Cys His Pro Asn Cys Thr Gln Gly
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Cys Asn Gly Pro Thr Ser His Asp Cys Ile Tyr Tyr Pro Trp Thr Gly
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His Ser Thr Leu Pro Gln His Ala Arg Thr Pro Leu Ile Ala Ala Gly
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Val Ile Gly Gly Leu Phe Ile Leu Val Ile Val Gly Leu Thr Phe Ala
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Val Tyr Val Arg Arg Lys Ser Ile Lys Lys Lys Arg Ala Leu Arg Arg
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Phe Leu Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly Thr Ala
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Pro Asn Gln Ala Gln Leu Arg Ile Leu Lys Glu Thr Glu Leu Lys Arg
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Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys Gly Ile
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Trp Val Pro Glu Gly Glu Thr Val Lys Ile Pro Val Ala Ile Lys Ile
740 745 750

Leu Asn Glu Thr Thr Gly Pro Lys Ala Asn Val Glu Phe Met Asp Glu
755 760 765

Ala Leu Ile Met Ala Ser Met Asp His Pro His Leu Val Arg Leu Leu
770 775 780

Gly Val Cys Leu Ser Pro Thr Ile Gln Leu Val Thr Gln Leu Met Pro
785 790 795 800

His Gly Cys Leu Leu Glu Tyr Val His Glu His Lys Asp Asn Ile Gly
805 810 815

Ser Gln Leu Leu Leu Asn Trp Cys Val Gln Ile Ala Lys Gly Met Met
820 825 830

Tyr Leu Glu Glu Arg Arg Leu Val His Arg Asp Leu Ala Ala Arg Asn
835 840 845

Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe Gly Leu
850 855 860

Ala Arg Leu Leu Glu Gly Asp Glu Lys Glu Tyr Asn Ala Asp Gly Gly
865 870 875 880

Lys Met Pro Ile Lys Trp Met Ala Leu Glu Cys Ile His Tyr Arg Lys
885 890 895

Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Ile Trp Glu
900 905 910

Leu Met Thr Phe Gly Gly Lys Pro Tyr Asp Gly Ile Pro Thr Arg Glu
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Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro Pro Ile
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Cys Thr Ile Asp Val Tyr Met Val Met Val Lys Cys Trp Met Ile Asp
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Met Lys Leu Pro Ser Pro Asn Asp Ser Lys Phe Phe Gln Asn Leu Leu
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Val Pro Gln Ala Phe Asn Ile Pro Pro Pro Ile Tyr Thr Ser Arg
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Pro Val Ala Pro His Val Gln Glu Asp Ser Ser Thr Gln Arg Tyr
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Ser Ala Asp Pro Thr Val Phe Ala Pro Glu Arg Ser Pro Arg Gly
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Glu Leu Asp Glu Glu Gly Tyr Met Thr Pro Met Arg Asp Lys Pro
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Lys Gln Glu Tyr Leu Asn Pro Val Glu Glu Asn Pro Phe Val Ser
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Arg Arg Lys Asn Gly Asp Leu Gln Ala Leu Asp Asn Pro Glu Tyr
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His Asn Ala Ser Asn Gly Pro Pro Lys Ala Glu Asp Glu Tyr Val
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Asn Glu Pro Leu Tyr Leu Asn Thr Phe Ala Asn Thr Leu Gly Lys
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Ala Glu Tyr Leu Lys Asn Asn Ile Leu Ser Met Pro Glu Lys Ala
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Lys Lys Ala Phe Asp Asn Pro Asp Tyr Trp Asn His Ser Leu Pro
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Pro Arg Ser Thr Leu Gln His Pro Asp Tyr Leu Gln Glu Tyr Ser
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Thr Lys Tyr Phe Tyr Lys Gln Asn Gly Arg Ile Arg Pro Ile Val
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Thr Val Cys Ala Gly Thr Glu Asn Lys Leu Ser Ser Leu Ser Asp Leu
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gaa cag cag tac cga gcc ttg cgc aaa tac tat gaa aac tgc gag gta 144
Glu Gln Gln Tyr Arg Ala Leu Arg Lys Tyr Tyr Glu Asn Cys Glu Val
35 40 45

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tac agg aaa gat ggc aac ttt gga ctc caa gaa ctt gga tta aag aac Tyr Arg Lys Asp Gly Asn Phe Gly Leu Gln Glu Leu Gly Leu Lys Asn 115 120 125	384
ctg acc gaa ata cta aat ggt gga gtc tat gta gac cag aac aaa ttc Leu Thr Glu Ile Leu Asn Gly Gly Val Tyr Val Asp Gln Asn Lys Phe 130 135 140	432
cta tgt tat gct gac act ata cac tgg caa gat att gtt cgg aat cca Leu Cys Tyr Ala Asp Thr Ile His Trp Gln Asp Ile Val Arg Asn Pro 145 150 155 160	480
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Gly His Ser Pro Pro Pro Ala	Tyr Thr Pro Met Ser	Gly Asn Gln	
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Phe Val Tyr Gln Asp Gly Gly	Phe Ala Thr Gln Gln	Gly Met Pro	
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Ala Gln Gly Ala Thr Ala Glu	Met Phe Asp Asp Ser	Cys Cys Asn	
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Ser Thr Gln Arg Tyr Ser Ala	Asp Pro Thr Val Phe	Ala Pro Glu	
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Arg Asn Pro Arg Gly Glu Leu	Asp Glu Glu Gly Tyr	Met Thr Pro	
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Met His Asp Lys Pro Lys Gln	Glu Tyr Leu Asn Pro	Val Glu Glu	
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Leu Gln	Glu Tyr Ser Thr Lys	Tyr Phe Tyr Lys	Gln Asn Gly Arg	
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Ile Arg	Pro Ile Val Ala Glu	Asn Pro Glu Tyr Leu	Ser Glu Phe	
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Ser Leu	Lys Pro Gly Thr Met	Leu Pro Pro Pro Pro	Tyr Arg His	
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 <213> Mus musculus

<400> 21

Met Ala	Ile Pro	Ser Arg	Arg Lys	Asp Tyr	Pro Lys	Leu Ser	Glu Ile
1	5			10		15	

Thr Val	Cys Ala	Gly Thr	Glu Asn	Lys Leu	Ser Ser	Leu Ser	Asp Leu
	20		25			30	

Glu Gln	Gln Tyr	Arg Ala	Leu Arg	Lys Tyr	Tyr Glu	Asn Cys	Glu Val
	35		40			45	

Val Met	Gly Asn	Leu Glu	Ile Thr	Ser Ile	Glu His	Asn Arg	Asp Leu
50		55			60		

Ser Phe	Leu Arg	Ser Ile	Arg Glu	Val Thr	Gly Tyr	Val Leu	Val Ala
65		70			75		80

Leu Asn	Gln Phe	Arg Tyr	Leu Pro	Leu Glu	Asn Leu	Arg Ile	Ile Arg
	85			90			95

Gly Thr	Lys Leu	Tyr Glu	Asp Arg	Tyr Ala	Leu Ala	Ile Phe	Leu Asn
	100			105		110	

Tyr Arg	Lys Asp	Gly Asn	Phe Gly	Leu Gln	Glu Leu	Gly Leu	Lys Asn
	115		120			125	

Leu Thr Glu Ile Leu Asn Gly Gly Val Tyr Val Asp Gln Asn Lys Phe
 130 135 140

Leu Cys Tyr Ala Asp Thr Ile His Trp Gln Asp Ile Val Arg Asn Pro
 145 150 155 160

Trp Pro Ser Asn Met Thr Leu Val Ser Thr Asn Gly Ser Ser Gly Cys
 165 170 175

Gly Arg Cys His Lys Ser Cys Thr Gly Arg Cys Trp Gly Pro Thr Glu
 180 185 190

Asn His Cys Gln Thr Leu Thr Arg Thr Val Cys Ala Glu Gln Cys Asp
 195 200 205

Gly Arg Cys Tyr Gly Pro Tyr Val Ser Asp Cys Cys His Arg Glu Cys
 210 215 220

Ala Gly Gly Cys Ser Gly Pro Lys Asp Thr Asp Cys Phe Ala Cys Met
 225 230 235 240

Asn Phe Asn Asp Ser Gly Ala Cys Val Thr Gln Cys Pro Gln Thr Phe
 245 250 255

Val Tyr Asn Pro Thr Thr Phe Gln Leu Glu His Asn Phe Asn Ala Lys
 260 265 270

Tyr Thr Tyr Gly Ala Phe Cys Val Lys Lys Cys Pro His Asn Phe Val
 275 280 285

Val Asp Ser Ser Ser Cys Val Arg Ala Cys Pro Ser Ser Lys Met Glu
 290 295 300

Val Glu Glu Asn Gly Ile Lys Met Cys Lys Pro Cys Thr Asp Ile Cys
 305 310 315 320

Pro Lys Ala Cys Asp Gly Ile Gly Thr Gly Ser Leu Met Ser Ala Gln
 325 330 335

Thr Val Asp Ser Ser Asn Ile Asp Lys Phe Ile Asn Cys Thr Lys Ile
 340 345 350

Asn Gly Asn Leu Ile Phe Leu Val Thr Gly Ile His Gly Asp Pro Tyr
 355 360 365

Asn Ala Ile Asp Ala Ile Asp Pro Glu Lys Leu Asn Val Phe Arg Thr
 370 375 380

Val Arg Glu Ile Thr Gly Phe Leu Asn Ile Gln Ser Trp Pro Pro Asn
 385 390 395 400

Met Thr Asp Phe Ser Val Phe Ser Asn Leu Val Thr Ile Gly Gly Arg
 405 410 415

Val Leu Tyr Ser Gly Leu Ser Leu Leu Ile Leu Lys Gln Gln Gly Ile
 420 425 430

Thr Ser Leu Gln Phe Gln Ser Leu Lys Glu Ile Ser Ala Gly Asn Ile
 435 440 445

Tyr Ile Thr Asp Asn Ser Asn Leu Cys Tyr Tyr His Thr Ile Asn Trp
 450 455 460

Thr Thr Leu Phe Ser Thr Ile Asn Gln Arg Ile Val Ile Arg Asp Asn
 465 470 475 480

Arg Arg Ala Glu Asn Cys Thr Ala Glu Gly Met Val Cys Asn His Leu
 485 490 495

Cys Ser Asn Asp Gly Cys Trp Gly Pro Gly Pro Asp Gln Cys Leu Ser
 500 505 510

Cys Arg Arg Phe Ser Arg Gly Lys Ile Cys Ile Glu Ser Cys Asn Leu
 515 520 525

Tyr Asp Gly Glu Phe Arg Glu Phe Glu Asn Gly Ser Ile Cys Val Glu
 530 535 540

Cys Asp Ser Gln Cys Glu Lys Met Glu Asp Gly Leu Leu Thr Cys His
 545 550 555 560

Gly Pro Gly Pro Asp Asn Cys Thr Lys Cys Ser His Phe Lys Asp Gly
 565 570 575

Pro Asn Cys Val Glu Lys Cys Pro Asp Gly Leu Gln Gly Ala Asn Ser
 580 585 590

Phe Ile Phe Lys Tyr Ala Asp Gln Asp Arg Glu Cys His Pro Cys His
 595 600 605

Pro Asn Cys Thr Gln Gly Cys Asn Gly Pro Thr Ser His Asp Cys Ile
610 615 620

Tyr Tyr Pro Trp Thr Gly His Ser Thr Leu Pro Gln His Ala Arg Thr
625 630 635 640

Pro Leu Ile Ala Ala Gly Val Ile Gly Gly Leu Phe Ile Leu Val Ile
645 650 655

Met Ala Leu Thr Phe Ala Val Tyr Val Arg Arg Lys Ser Ile Lys Lys
660 665 670

Lys Arg Ala Leu Arg Arg Phe Leu Glu Thr Glu Leu Val Glu Pro Leu
675 680 685

Thr Pro Ser Gly Thr Ala Pro Asn Gln Ala Gln Leu Arg Ile Leu Lys
690 695 700

Glu Thr Glu Leu Lys Arg Val Lys Val Leu Gly Ser Gly Ala Phe Gly
705 710 715 720

Thr Val Tyr Lys Gly Ile Trp Val Pro Glu Gly Glu Thr Val Lys Ile
725 730 735

Pro Val Ala Ile Lys Ile Leu Asn Glu Thr Thr Gly Pro Lys Ala Asn
740 745 750

Val Glu Phe Met Asp Glu Ala Leu Ile Met Ala Ser Met Asp His Pro
755 760 765

His Leu Val Arg Leu Leu Gly Val Cys Leu Ser Pro Thr Ile Gln Leu
770 775 780

Val Thr Gln Leu Met Pro His Gly Cys Leu Leu Asp Tyr Val His Glu
785 790 795 800

His Lys Asp Asn Ile Gly Ser Gln Leu Leu Leu Asn Trp Cys Val Gln
805 810 815

Ile Ala Lys Gly Met Met Tyr Leu Glu Glu Arg Arg Leu Val His Arg
820 825 830

Asp Leu Ala Ala Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys
835 840 845

Ile Thr Asp Phe Gly Leu Ala Arg Leu Leu Glu Gly Asp Glu Lys Glu
850 855 860

Tyr Asn Ala Asp Gly Gly Lys Met Pro Ile Lys Trp Met Ala Leu Glu
865 870 875 880

Cys Ile His Tyr Arg Lys Phe Thr His Gln Ser Asp Val Trp Ser Tyr
885 890 895

Gly Val Thr Ile Trp Glu Leu Met Thr Phe Gly Gly Lys Pro Tyr Asp
900 905 910

Gly Ile Pro Thr Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg
915 920 925

Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr Met Val Met Val
930 935 940

Lys Cys Trp Met Ile Asp Ala Asp Ser Arg Pro Lys Phe Lys Glu Leu
945 950 955 960

Ala Ala Glu Phe Ser Arg Met Ala Arg Asp Pro Gln Arg Tyr Leu Val
965 970 975

Ile Gln Gly Asp Asp Arg Met Lys Leu Pro Ser Pro Asn Asp Ser Lys
980 985 990

Phe Phe Gln Asn Leu Leu Asp Glu Glu Asp Leu Glu Asp Met Met Asp
995 1000 1005

Ala Glu Glu Tyr Leu Val Pro Gln Ala Phe Asn Ile Pro Pro Pro
1010 1015 1020

Ile Tyr Thr Ser Arg Thr Arg Ile Asp Ser Asn Arg Ser Glu Ile
1025 1030 1035

Gly His Ser Pro Pro Pro Ala Tyr Thr Pro Met Ser Gly Asn Gln
1040 1045 1050

Phe Val Tyr Gln Asp Gly Gly Phe Ala Thr Gln Gln Gly Met Pro
1055 1060 1065

Met Pro Tyr Arg Ala Thr Thr Ser Thr Ile Pro Glu Ala Pro Val
1070 1075 1080

Ala	Gln	Gly	Ala	Thr	Ala	Glu	Met	Phe	Asp	Asp	Ser	Cys	Cys	Asn
1085						1090					1095			
Gly	Thr	Leu	Arg	Lys	Pro	Val	Ala	Pro	His	Val	Gln	Glu	Asp	Ser
1100						1105					1110			
Ser	Thr	Gln	Arg	Tyr	Ser	Ala	Asp	Pro	Thr	Val	Phe	Ala	Pro	Glu
1115						1120					1125			
Arg	Asn	Pro	Arg	Gly	Glu	Leu	Asp	Glu	Glu	Gly	Tyr	Met	Thr	Pro
1130						1135					1140			
Met	His	Asp	Lys	Pro	Lys	Gln	Glu	Tyr	Leu	Asn	Pro	Val	Glu	Glu
1145						1150					1155			
Asn	Pro	Phe	Val	Ser	Arg	Arg	Lys	Asn	Gly	Asp	Leu	Gln	Ala	Leu
1160						1165					1170			
Asp	Asn	Pro	Glu	Tyr	His	Ser	Ala	Ser	Ser	Gly	Pro	Pro	Lys	Ala
1175						1180					1185			
Glu	Asp	Glu	Tyr	Val	Asn	Glu	Pro	Leu	Tyr	Leu	Asn	Thr	Phe	Ala
1190						1195					1200			
Asn	Ala	Leu	Gly	Ser	Ala	Glu	Tyr	Met	Lys	Asn	Ser	Val	Leu	Ser
1205						1210					1215			
Val	Pro	Glu	Lys	Ala	Lys	Lys	Ala	Phe	Asp	Asn	Pro	Asp	Tyr	Trp
1220						1225					1230			
Asn	His	Ser	Leu	Pro	Pro	Arg	Ser	Thr	Leu	Gln	His	Pro	Asp	Tyr
1235						1240					1245			
Leu	Gln	Glu	Tyr	Ser	Thr	Lys	Tyr	Phe	Tyr	Lys	Gln	Asn	Gly	Arg
1250						1255					1260			
Ile	Arg	Pro	Ile	Val	Ala	Glu	Asn	Pro	Glu	Tyr	Leu	Ser	Glu	Phe
1265						1270					1275			
Ser	Leu	Lys	Pro	Gly	Thr	Met	Leu	Pro	Pro	Pro	Pro	Tyr	Arg	His
1280						1285					1290			
Arg	Asn	Thr	Val	Val										
1295														